

FIG.1

ADAMTS-E nucleotide sequence [SEQ ID NO: 1]

CACGCGTCCGACGGCGCGGAGGCCCGGGCGGCGCAGGAGCCCGGTGAT
5 GCTGCGAAGGCTGTGAACAGGGGAGGCGGCACTGTGGGGGCTGCCGGCAGCCGGGG
CTGGGGAGAGACATGTGGACACGTGGCCTCTATGGCTCCCGCCTGCCAGATCCTCCGC
TGGGCCCTCGCCCTGGGGCTGGGCCTCATGTTGAGGTCACGCACGCCCTCCGGTCTC
AAGATGAGTTCCTGTCCAGTCTGGAGAGCTATGAGATCGCCTTCCCCACCCGCGTGGAC
CACAACGGGGCACTGCTGGCCTTCTCGCCACCTCCTCCCCGGAGGCAGCGCCGCGGC
10 ACGGGGGCCACAGCCGAGTCCCGCCTCTTCTACAAAGTGGCCTCGCCCAGCACCCACT
TCCTGCTGAACCTGACCCGCAGCTCCCGTCTACTGGCAGGGCACGTCTCCGTGGAGTA
CTGGACACGGGAGGGCCTGGCCTGGCAGAGGGCGGCCCGGCCCACTGCCTCTACGC
TGGTCACCTGCAGGGCCAGGCCAGCACCTCCCATGTGGCCATCAGCACCTGTGGAGGC
CTGCACGGCCTGATCGTGGCAGACGAGGAAGAGTACCTGATTGAGCCCCTGCACGGTG
15 GGCCCAAGGGTTCTCGGAGCCCGGAGGAAAGTGGACCACATGTGGTGTACAAGCGTTC
CTCTCTGCGTCACCCCCACCTGGACACAGCCTGTGGAGTGAGAGATGAGAAACCGTGG
AAAGGGCGGCCATGGTGGCTGCGGACCTTGAAGCCACCGCCTGCCAGGCCCTGGGG
AATGAAACAGAGCGTGGCCAGCCAGGCCTGAAGCGATCGGTGAGCCGAGAGCGCTACG
TGGAGACCCTGGTGGTGGCTGACAAGATGATGGTGGCCTATCACGGGCGCCGGGATGT
20 GGAGCAGTATGTCTGGCCATCATGAACATTGTTGCCAAACTTTTCCAGGACTCGAGTCT
GGGAAGCACCGTTAACATCCTCGTAACTCGCCTCATCCTGCTCACGGAGGACCAGCCCA
CTCTGGAGATCACCCACCATGCCGGGAAGTCCCTGGACAGCTTCTGTAAGTGGCAGAAA
TCCATCGTGAACCACAGCGGCCATGGCAATGCCATTCCAGAGAACGGTGTGGCTAACCA
TGACACAGCAGTGCTCATCACACGCTATGACATCTGCATCTACAAGAACAAACCCTGCG
25 GCACACTAGGCCTGGCCCCGGTGGGCGGAATGTGTGAGCGCGAGAGAAGCTGCAGCG
TCAATGAGGACATTGGCCTGGCCACAGCGTTACCATTTGCCACGAGATCGGGCACACA
TTCGGCATGAACCATGACGGCGTGGGAAACAGCTGTGGGGCCCGTGGTCAGGACCCAG
CCAAGCTCATGGCTGCCACATTACCATGAAGACCAACCCATTTCGTGTGGTCATCCTGC
AGCCGTGACTACATCACCAGCTTTCTAGACTCGGGCCTGGGGCTCTGCCTGAACAACCG
30 GCCCCCAGACAGGACTTTGTGTACCCGACAGTGGCACCGGGCCAAGCCTACGATGCA
GATGAGCAATGCCGCTTTCAGCATGGAGTCAAATCGCGTCAGTGTAATACGGGGAGGT
CTGCAGCGAGCTGTGGTGTCTGAGCAAGAGCAACCGGTGCATCACCAACAGCATCCCG
GCCGCCGAGGGCACGCTGTGCCAGACGCACACCATCGACAAGGGGTGGTGTACAAAC
GGGTCTGTGTCCCTTTGGGTGCGGCCAGAGGGTGTGGACGGAGCCTGGGGGCCGT
35 GGACTCCATGGGGCGACTGCAGCCGACCTGTGGCGGCGGCGTGTCTCTTCTAGCC
GTCACTGCGACAGCCCCAGGCCAACCATCGGGGGCAAGTACTGTCTGGGTGAGAGAAG
GCGGCACCGCTCCTGCAACACGGATGACTGTCCCCCTGGCTCCAGGACTTCAGAGAA

EXPRESS MAIL NO. EL446402267 US

GTGCAGTGTTCTGAATTTGACAGCATCCCTTTCCGTGGGAAATTCTACAAGTGGAAAACG
TACCGGGGAGGGGGCGTGAAGGCCTGCTCGCTCACGTGCCTAGCGGAAGGCTTCAACT
TCTACACGGAGAGGGCGGCAGCCGTGGTGGACGGGACACCCTGCCGTCCAGACACGG
TGGACATTTGCGTCAGTGGCGAATGCAAGCACGTGGGCTGCGACCGAGTCCTGGGCTC
5 CGACCTGCGGGAGGACAAGTGCCGAGTGTGTGGCGGTGACGGCAGTGCCTGCGAGAC
CATCGAGGGCGTCTTCAGCCCAGCCTCACCTGGGGCCGGGTACGAGGATGTCGTCTGG
ATTCCTCAAAGGCTCCGTCCACATCTTCATCCAGGATCTGAACCTCTCTCTCAGTCACTTG
GCCCTGAAGGGAGACCAGGAGTCCCTGCTGCTGGAGGGGCTGCCCGGGACCCCCCAG
CCCCACCGTCTGCCTCTAGCTGGGACCACCTTTCAACTGCGACAGGGGCCAGACCAGG
10 TCCAGAGCCTCGAAGCCCTGGGACCGATTAATGCATCTCTCATCGTCATGGTGCTGGCC
CGGACCGAGCTGCCTGCCCTCCGCTACCGCTTCAATGCCCCCATCGCCCGTGACTCGC
TGCCCCCCTACTCCTGGCACTATGCGCCCTGGACCAAGTGCTCGGCCCAAGTGTGCAGG
CGGTAGCCAGGTGCAGGCGGTGGAGTGCCGCAACCAGCTGGACAGCTCCGCGGTGCG
CCCCCACTACTGCAGTGCCCACAGCAAGCTGCCCAAAAGGCAGCGCGCCTGCAACACG
15 GAGCCTTGCCCTCCAGACTGGGTTGTAGGGAAGTGGTCGCTCTGCAGCCGCAGCTGCG
ATGCAGGCGTGCGCAGCCGCTCGGTCTGTGTGCCAGCGCCGCGTCTCTGCCGCGGAGG
AGAAGGCGCTGGACGACAGCGCATGCCCGCAGCCGCGCCACCTGTACTGGAGGCCT
GCCACGGCCCCACTTGCCCTCCGGAGTGGGCGGCCCTCGACTGGTCTGAGTGCACCC
CCAGCTGCGGGCCGGGCCTCCGCCACCGCGTGGTCCTTTGCAAGAGCGCAGACCACC
20 GCGCCACGCTGCCCCCGGCGCACTGCTCACCCGCCGCCAAGCCACCGGCCACCATGC
GCTGCAACTTGCGCCGCTGCCCCCGGCCGCTGGGTGGCTGGCGAGTGGGGTGAGT
GCTCTGCACAGTGCGGCGTCGGGCAGCGGCAGCGCTCGGTGCGCTGCACCAGCCACA
CGGGCCAGGCGTCGCACGAGTGACGGAGGCCCTGCGGCCGCCGACTACCACGCAGC
AGTGTGAGGCCAAGTGCGACAGCCCAACCCCCGGGGACGGCCCTGAAGAGTGCAAGG
25 ATGTGAACAAGGTCGCCTACTGCCCCCTGGTGCTCAAATTTAGTTCTGCAGCCGAGCC
TACTTCCGCCAGATGTGCTGCAAAACCTGCCAGGGGCCACTAGGGGGCGCGCGGCACCC
GGAGCCACAGCTGGCGGGGTCTCCGCCGCCAGCCCTGCAGCGGGCCGGCCAGAGGG
GGCCCCGGGGGGGGCGGGAAGTGGGAGGGAAGGGTGAGACGGAGCCGGAAGTTATTT
ATTGGGAACCCCTGCAGGGCCCTGGCTGGGAGGATCCACCCCAACCTCTGCCCTGCC
30 GCCCCAGGGGCACCCCGACATCCAGGCCACCCCTCATGGTGCTACAGACCCTGCCCT
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TTCTAAAAAAAAAAAAAA

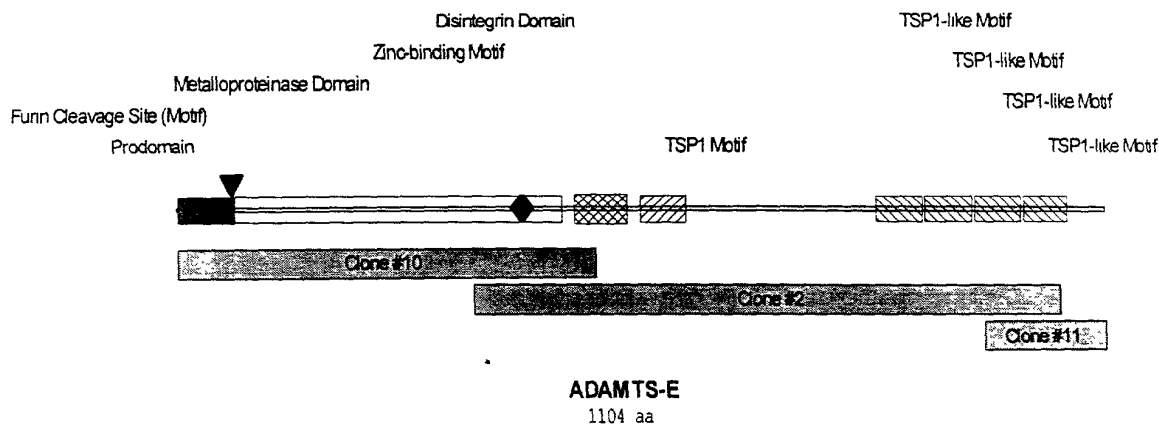
FIG 2

ADAMTS-E amino acid sequence [SEQ ID NO: 2]

MAPACQILRWALALGLGLMFEVTHAFRSQDEFLSSLESYEIAFPTRVDHNGALLAFS
PPPPRRQRRGTGATAESRLFYKVASPTHFLLNLTRSSRLLAGHVSVEYWTREGLA
5 WQRAARPHCLYAGHLQGGQASTSHVAISTCGGLHGLLIVADEEEYLIEPLHGGPKGSR
SPEESGPHVVYKRSSLRHPHLDTACGVRDEKPKWGRPWWLRTLKPPPARPLGNE
TERGQPGLKRSVSRERYVETLVVADKMMVAYHGRRDVEQYVLAIMNIVAKLFQDSS
LGSTVNILVTRLILLTQPTLEITHHAGKSLDSFCKWQKSIVNHSGHGNAPENGVA
NHDTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCSVNEDIGLATAFTIAHEIG
10 HTFGMNHDGVGNSCGARGQDPAKLMAAHITMKTNPFWSSCSRDIYSFLDSGLG
LCLNNRPPRQDFVYPTVAPGQAYDADEQCRFQHGVKSRQCKYGEVCSELWCLSK
SNRCITNSIPAAEGTLCQTHIDKGWCYKRVCPFGSRPEGVDGAWGPWTPWGDG
SRTC GGGVSSSSRHCDSPRPTIGGKYCLGERRRHRSCNTDDCPPGSQDFREVQC
SEFDSIPFRGKFYKWKTYRGGGVKACSLTCLAEGFNFYTERAAAVDGTPCRPTV
15 DICVSGECKHVGCDRVLGSDLREDKCRVCGGDGSACETIEGVFSPASPGAGYEDV
VWIPKGSVHIFIQDLNLSLSHLALKGDQESLLEGLPGTPQPHRLPLAGTTFQLRQGP
DQVQSLEALGPINASLIVMVLARTELPALRYRFNAPIARDSLPPYSWHYAPWTKCSA
QCAGGSQVQAVECRNQLDSSAVAPHYCSAHSKLPKRQRACNTEPCPPDWVGN
WSLCSRSCDAGVRSRSVVCQRRVSAAEEKALDDSA CPQPRPPVLEACHGPTCPPE
20 WAALDWSECTPSCGPGLRHRVVLCKSADHRATLPPAHCSAAKPPATMRCNLRRRC
PPARWWAGEWGECSAQCGVGQRQRSVRCTSHTGQASHECTEALRPPTTTQQCE
AKCDSPTPGDGPEECKDVNKVAYCPLVLKFQFCRAYFRQMCCCKTCQGH

Figure 3. Domain structure of ADAMTS-E and translated nucleic acid sequence. A) Diagram of ADAMTS-E showing the following domains and signature motifs (with amino acid numbers in parentheses): prodomain (1-66), furin cleavage site (63-66), metalloproteinase domain (67-453), zinc-binding motif (392-420), disintegrin domain (469-531), TSP1 motif (548-601), and four TSP1-like motifs (829-884, 888-944, 948-1002, and 1007-1058). Overlapping clones covering the indicated sequence segments are depicted at the bottom of the diagram. **B)** ADAMTS-E nucleotide sequence with translated amino acid sequence above.

A



B

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1  CACGCGTCCG ACGGCGCGGA GGCCCGGGC GCGGCGCAGG AGCCCGGTGA TGCTGCGAAG GCTGTGAACA GGGGAGGCGG
   GTGCGCAGGC TGCCGCGCCT CCGGGGCCCG CGCCGCGTCC TCGGGCCACT ACGACGCTTC CGACACTTGT CCCCTCCGCC

+1                                     M  A  P  A  C  Q  I
                                     =====
                                     Prodomain

81  CACTGTGGGG GCTGCCGGCA GCCGGGGCTG GGGAGAGACA TGTGGACACG TGGCCTCTAT GGCTCCCGCC TGCCAGATCC
   GTGACACCCC CGACGGCCGT CGGCCCGGAC CCCTCTCTGT ACACCTGTGC ACCGGAGATA CCGAGGGCGG ACGGTCTAGG

+1  L  R  W  A  L  A  L  G  L  G  L  M  F  E  V  T  H  A  F  R  S  Q  D  E  F  L  S
                                     =====
                                     Prodomain

161 TCCGCTGGGC CCTCGCCCTG GGGCTGGGCC TCATGTTCTGA GGTACGCGAC GCCTTCCGGT CTCAAGATGA GTTCTGTCC
   AGGCGACCCG GGAGCGGGAC CCCGACCCGG AGTACAAGCT CCAGTGCGTG CGGAAGGCCA GAGTTCTACT CAAGGACAGG

+1  S  L  E  S  Y  E  I  A  F  P  T  R  V  D  H  N  G  A  L  L  A  F  S  P  P  P  P
   Prodomain
   =====

241 AGTCTGGAGA GCTATGAGAT CGCCTTCCCC ACCCGCGTGG ACCACAACGG GGCAGTGTG GCCTTCTCGC CACCTCCTCC
   TCAGACCTCT CGATACTCTA GCGGAAGGGG TGGGCGCACC TGGTGTGCC CCGTGACGAC CGGAAGAGCG GTGGAGGAGG

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+1 R R Q R R G T G A T A E S R L F Y K V A S P S T H F
Furin Cleavage Site (Motif)
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Prodomain                               Metalloproteinase Domain
=====
321 CCGGAGGCAG CGCCGCGGCA CGGGGGCCAC AGCCGAGTCC CGCCTCTTCT ACAAAGTGGC CTCGCCCAGC ACCCAATTCT
    GGCCTCCGTC GCGGCGCCGT GCCCCCGGTG TCGGCTCAGG GCGGAGAAGA TGTTCACCG GAGCGGGTCG TGGSTCAACC

+1 L L N L T R S S R L L A G H V S V E Y W T R E G L A A
                                           Metalloproteinase Domain
=====
401 TGCTGAACCT GACCCGCAGC TCCCGTCTAC TGGCAGGGCA CGTCTCCGTG GAGTACTGGA CACGGGAGGG CCTGGCCTGG
    ACGACTTGGA CTGGGCGTCG AGGCGAGATG ACCGTCCCGT GCAGAGGCAC CTCATGAOCT GTGCCCTCCC GGACCGGACT

+1 Q R A A R P H C L Y A G H L Q G Q A S T S H V A I S T
                                           Metalloproteinase Domain
=====
481 CAGAGGGCGG CCGGGCCCCA CTGCCTCTAC GCTGGTCACC TGCAGGGCCA GGCCAGCACC TCCCATGTGG CCATCAGCAC
    GTCTCCCGCC GGGCCGGGGT GACGGAGATG CGACCACTGG ACGTCCCGGT CCGGTCGTGG AGGGTACACC GGTAGTCTGT

+1 C G G L H G L I V A D E E E Y L I E P L H G G P K G
                                           Metalloproteinase Domain
=====
561 CTGTGGAGGC CTGCACGGCC TGATCGTGGC AGACAGGAA GAGTACCTGA TTGAGCCCCT GCACGGTGGG CCCAAGGCTT
    GACACCTCCG GACGTGCCGG ACTAGCACCG TCTGCTCCTT CTCATGGACT AACTCGGGGA CGTGCCACCC GGGTTCGCAA

+1 S R S P E E S G P H V V Y K R S S L R H P H L D T A T
                                           Metalloproteinase Domain
=====
641 CTCGGAGCCC GGAGGAAAGT GGACCACATG TGGTGTACAA GCGTTCCTCT CTGCGTCACC CCCACCTGGA CACAGCCTGT
    GAGCCTCGGG CCTCCTTTCA CCTGGGTGAC ACCACATGTT CGCAAGGAGA GACGCAGTGG GGGTGGACCT GTGTGCGACA

+1 G V R D E K P W K G R P W W L R T L K P P P A R P L G
                                           Metalloproteinase Domain
=====
721 GGAGTGAGAG ATGAGAAACC GTGGAAAGGG CGGCCATGGT GGCTGCGGAC CTTGAAGCCA CGCCTGCCA GGCCCTGGG
    CCTCACTCTC TACTCTTTGG CACCTTTCCC GCCGGTACCA CCGACGCTG GAACTTCGGT GCGGACGGT CCGGGGACCC

+1 N E T E R G Q P G L K R S V S R E R Y V E T L V V A
                                           Metalloproteinase Domain
=====
801 GAATGAAACA GAGCGTGGCC AGCCAGGCCT GAAGCGATCG GTCAGCCGAG AGCGCTACGT GGAGACCCCTG GTGGTGGCTG
    CTTACTTTGT CTCGCACCGG TCGGTCCGGA CTTGCTAGC CAGTCGGCTC TCGCGATGCA CCTCTGGGAC CACCACCGAC

+1 D K M M V A Y H G R R D V E Q Y V L A I M N I V A K L
                                           Metalloproteinase Domain
=====
881 ACAAGATGAT GGTGGCCTAT CACGGGCGCC GGGATGTGGA GCAGTATGTC CTGGCCATCA TGAACATTGT TGCCAACTT
    TGTCTACTA CCACCGGATA GTGCCCGCGG CCCTACACCT CGTCATACAG GACCGGTAGT ACTTGTAACA ACGGTTTGAA

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+1 F Q D S S L G S T V N I L V T R L I L L T E D Q P T L
Metalloproteinase Domain
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961 TTCCAGGACT CGAGTCTGGG AAGCACCGTT AACATCCTCG TAACTCGCCT CATCCTGCTC ACGGAGGACC AGCCCACTCT
AAGGTCCTGA GCTCAGACCC TTCGTGGCAA TTGTAGGAGC ATTGAGCGGA GTAGGACGAG TGCCTCCTGG TCGCGTGAGA

+1 E I T H H A G K S L D S F C K W Q K S I V N H G
Metalloproteinase Domain
=====
1041 GGAGATCACC CACCATGCCG GGAAGTCCCT GGACAGCTTC TGTAAGTGGC AGAAATCCAT CGTGAACCCAC AGCGGCCCATG
CCTCTAGTGG GTGGTACGGC CCTTCAGGGA CCTGTGGAAG ACATTCACCG TCCTTAGGTA GCACTTGGTG TCGCCGGTAC

+1 G N A I P E N G V A N H D T A V L I T R Y D I C I Y K
Metalloproteinase Domain
=====
1121 GCAATGCCAT TCCAGAGAAC GGTGTGGCTA ACCATGACAC GCAGTGGCTC ATCACACGCT ATGACATCTG CATCTACAGG
CGTTACGGTA AGGTCTCTTG CCACACCGAT TGGTACTGTG CGTCACGAG TAGTGTGCGA TACTGTAGAC GTAGAIGTTC

+1 N K P C G T L G L A P V G G M C E R E R S C S V N E D
Metalloproteinase Domain
=====
1201 AACAAACCCT GCGGCACACT AGGCCTGGCC CCGGTGGGCG GAATGTGTGA GCGCGAGAGA AGCTGCAGCG TCAATGAGGA
TTGTTTGGGA CGCCGTGTGA TCCGGACCGG GGCCACCCCG CTTACACACT CGCGCTCTCT TCGACGTCGC AGTTACTCCT

+1 I G L A T A F T I A H E I G H T F G M N H D G V G N
Zinc-binding Motif
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Metalloproteinase Domain
=====
1281 CATTGGCCTG GCCACAGCGT TCACCATGTC CCACGAGATC GGGCACACAT TCGGCATGAA CCATGACGGC GTGGGAAACA
GTAACCGGAC CGGTGTCGCA AGTGGTAACG GGTGCTCTAG CCCGTGTGTA AGCCGTACTT GGTACTGCCG CACCCCTTGT

+1 S C G A R G Q D P A K L M A A H I T M K T N P F V W S
Zinc-binding Motif
=====
Metalloproteinase Domain
=====
1361 GCTGTGGGGC CCGTGGTCAG GACCCAGCCA AGCTCATGGC TGCCACATT ACCATGAAGA CCAACCCATT CGTGTGGTCA
CGACACCCCG GGCACCACTC CTGGGTCGGT TCGAGTACCG ACGGGTGTA TGGTACTTCT GGTGGGTAA GCACACCACT

+1 S C S R D Y I T S F L D S G L G L C L N N R P P R Q D
Metalloproteinase Domain
=====
1441 TCCTGCAGCC GTGACTACAT CACCAGCTTT CTAGACTCGG GCCTGGGGCT CTGCCTGAAC AACCGGCCCC CCAGACAGGA
AGGACGTCGG CACTGATGTA GTGGTCGAAA GATCTGAGCC CGGACCCCGA GACGGACTTG TTGGCCGGGG GGTCTGTCTT

+1 F V Y P T V A P G Q A Y D A D E Q C R F Q H G V K S
Disintegrin Domain
=====
1521 CTTTGTGTAC CCGACAGTGG CACCGGGCCA AGCCTACGAT GCAGATGAGC AATGCCGCTT TCAGCATGGA GTCAAATCGC
GAAACACATG GGCTGTACAC GTGGCCCGGT TCGGATGCTA CGTCTACTCG TTACGGCGAA AGTCGTACCT CAGTTTAGCG
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+1 R Q C K Y G E V C S E L W C L S K S N R C I T N S I P
Disintegrin Domain

1601 GTCAGTGTA ATACGGGGAG GTCTGCAGCG AGCTGTGGTG TCTGAGCAAG AGCAACCGGT GCATCACCAA CAGCATCCCC
CAGTCACATT TATGCCCCCTC CAGACGTCGC TCGACACCAC AGACTCGTTC TCGTTGGCCA CGTAGTGGTT GTGGT-GGCG

+1 A A E G T L C Q T H T I D K G W C Y K R V C V P F E S
Disintegrin Domain

1681 GCCGCCGAGG GCACGCTGTG CCAGACGCAC ACCATCGACA AGGGGTGGTG CTACAAACGG GTCTGTGTCC CCTTTGGGTG
CGCGGGCTCC CGTGGCACAC GGTCTGCGTG TGGTAGCTGT TCCCCACCAC GATGTTGCC CAGACACAGG GGAAACCCAG

+1 R P E G V D G A W G P W T P W G D C S R T C G G S V
TSPI Motif

1761 GCGCCAGAG GGTGTGGACG GAGCCTGGGG GCCGTGGACT CCATGGGGCG ACTGCAGCCG GACCTGTGGC GGCGGCTGT
CGCGGGTCTC CCACACCTGC CTCGGACCCC CGGCACCTGA GGTACCCCGC TGACGTCGGC CTGGACACCG CGCGCGCACA

+1 S S S S R H C D S P R P T I G G K Y C L G E R R R H R
TSPI Motif

1841 CCTCTTCTAG CCGTCACTGC GACAGCECCA GGCCAACCAT CGGGGGCAAG TACTGTCTGG GTGAGAGAAG GCGGCACCGC
GGAGAAGATC GGCAGTGACG CTGTCGGGGT CCGGTTGGTA GCCCCCGTTC ATGACAGACC CACTCTCTTC CGCGGTGGCG

+1 S C N T D D C P P G S Q D F R E V Q C S E F D S I P F
TSPI Motif

1921 TCCTGCAACA CGGATGACTG TCCCCCTGGC TCCCAGGACT TCAGAGAAGT GCAGTGTCTT GAATTGACA GCATCCCTTT
AGGACGTTGT GCCTACTGAC AGGGGGACCG AGGGTCTGA AGTCTCTTCA CGTCACAAGA CTAAACTGT CGTAGGGA

2001 CCGTGGGAAA TTCTACAAGT GGAAACGTA CCGGGGAGGG GCGGTGAAGG CCTGCTCGCT CACGTGCCTA GCGGAAGGGT
GGCACCCCTTT AAGATGTTCA CCTTTGTCAT GGCCCCCTCC CCGCACTTCC GGACGAGCGA GTGCACGGAT CGCCTTCGGA

2081 TCAACTTCTA CACGGAGAGG GCGGCAGCCG TGGTGGACGG GACACCCTGC CGTCCAGACA CGGTGGACAT TTGCGTCAGT
AGTTGAAGAT GTGCCTCTCC CGCCGTCGGC ACCACCTGCC CTGTGGGACG GCAGGTCTGT GCCACCTGTA AACGCAGTCA

2161 GGCGAATGCA AGCACGTGGG CTGCGACCGA GTCCTGGGCT CCGACCTGCG GGAGGACAAG TGCCGAGTGT GTGGCGGTGA
CCGCTTACGT TCGTGCACCC GACGCTGGCT CAGGACCCGA GGCTGGACGC CCTCCTGTTT ACGGCTCACA CACCGCCACT

2241 G S A C E T I E G V F S P A S P G A G Y E D V V W I
CGGCAGTGCC TCGGAGACCA TCGAGGGCGT CTTCAGCCCA GCCTCACCTG GGGCCGGGTA CGAGGATGTC GTCTGGATTC
GCCGTCACGG ACGCTCTGGT AGCTCCCGCA GAAGTCGGGT CGGAGTGGAC CCCGGCCCAT GTCCTACAG CAGACCTAAG

2321 C C A A A G G C T C C G T C C A T C T T C A T C C A G G A T C T C T C A G T C A C T T G G C C C T G A A G G G A G A C C A G G A G T C C
G G T T T C C G A G C A G G T G T A G A A G T A G T C C T A G A C T T G G A G A G A G T C A G T A A C C G G G A C T T C C C T C T G G T C C A G G

2401 L L L E G L P G T P Q P H R L P L A G T T F Q L R Q G
CTGCTGCTGG AGGGGCTGCC CGGGACCCCC CAGCCCCACC GTCTGCCTCT AGCTGGGACC ACCTTTCAAC TGCGACAGGG
GACGACGACC TCCCCGACGG GCCCTGGGGG GTCGGGGTGG CAGACGGAGA TCGACCCTGG TGGAAAGTTG ACGCTGTCCC

+1 P D Q V Q S L E A L G P I N A S L I V M V L A R T E
 2481 GCCAGACCAG GTCCAGAGCC TCGAAGCCCT GGGACCGATT AATGCATCTC TCATCGTCAT GGTGCTGGCC CGGACCGAGC
CGGTCTGGTC CAGGTCTCGG AGCTTCGGGA CCCTGGCTAA TTACGTAGAG AGTAGCAGTA CCACGACCGG CCCTGGCTCG

+1 L P A L R Y R F N A P I A R D S L P P Y S W H Y A P W
 TSPl-like Motif
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2561 TGCCTGCCCT CCGCTACCGC TTCAATGCCC CCATCGCCCG TGACTCGCTG CCCCCCTACT CCTGGCACTA TGCGCCCTCG
ACGGACGGGA GCGCATGGCG AAGTTACGGG GGTAGCGGGC ACTGAGCGAC GGGGGGATGA GGACCGTGAT ACGCGGGAGC

+1 T K C S A Q C A G G S Q V Q A V E C R N Q L D S S A V
 TSPl-like Motif
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2641 ACCAAGTGCT CGGCCAGTG TGCAGGCGGT AGCCAGGTGC AGGCGGTGGA GTGCCGCAAC CAGCTGGACA GCTCCGCGCT
TGGTTCACGA GCCGGGTCAC ACGTCCGCCA TCGGTCCACG TCCGCCACCT CACGGCGTTG GTCGACCTGT CGAGGCGCTG

+1 A P H Y C S A H S K L P K R Q R A C N T E P C P P C
 TSPl-like Motif TSPl-like Motif
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2721 CGCCCCCAC TACTGCAGTG CCCACAGCAA GCTGCCAAA AGGCAGCGCG CCTGCAACAC GGAGCCTTGC CCTCCAGACT
GCGGGGGGTG ATGACGTCAC GGGTGTCTGT CGACGGGTTT TCCGTCGCGC GGACGTTGTG CCTCGGAACG GGAGGTCTGA

+1 W V V G N W S L C S R S C D A G V R S R S V V C Q R R
 TSPl-like Motif
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2801 GGGTGTAGG GAACTGGTCG CTCTGCAGCC GCAGCTGCGA TGCAGGCGTG CGCAGCCGCT CGGTCTGTG CCAGCGCGCG
CCCAACATCC CTTGACCAGC GAGACGTCGG CGTCGACGCT ACGTCCGCAC GCGTCGGCGA GCCAGCACAC GGTGCGCGCG

+1 V S A A E E K A L D D S A C P Q P R P P V L E A C H G
 TSPl-like Motif
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2881 GTCTCTGCCG CGGAGGAGAA GCGCTGGAC GACAGCGCAT GCCCGCAGCC GCGCCACCT GTACTGGAGG CCTGCCACGG
CAGAGACGGC GCCTCCTCTT CCGCGACCTG CTGTCGCGTA CGGGCGTCGG CGCGGGTGA CATGACCTCC GGACGGTCCG

+1 P T C P P E W A A L D W S E C T P S C G P G L R H R
 TSPl-like Motif TSPl-like Motif
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2961 CCCCACTTGC CCTCCGAGT GGGCGGCCCT CGACTGGTCT GAGTGCACCC CCAGCTGCGG GCCGGGCTC CGCCACCGCG
GGGGTGAACG GGAGGCCTCA CCCGCCGGA GCTGACCAGA CTCACGTGGG GGTGACGCC CGGCCCGGAG GCGGTGGCGC

+1 V V L C K S A D H R A T L P P A H C S P A A K P P A T
 TSPl-like Motif
 =====

3041 TGGTCCTTTG CAAGAGCGCA GACCACCGCG CCACGCTGCC CCCGGCGCAC TGCTACCCG CCGCCAAGCC ACCGGCCACC
ACCAGGAAAC GTTCTCGCGT CTGGTGGCGG GGTGCGACGG GGGCCGCGTG ACGAGTGGG GCGGTTCTGG TGGCGGTGG

+1 M R C N L R R C P P A R W V A G E W G E C S A Q C G V
 TSPl-like Motif TSPl-like Motif
 =====

3121 ATGCGCTGCA ACTTGCGCG CTGCCCCCGG GCCCGCTGGG TGGCTGGCGA GTGGGGTGAG TGCTCTGCAC AGTGGCGCGT
TACGCGACGT TGAACGCGGC GACGGGGGGC CGGGCGACCC ACCGACCGCT CACCCCACTC ACGAGACGTG TCACGCCGCA

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3201  C G G G C A G C G G  C A G C G C T C G G  T G C G C T G C A C  C A G C C A C A C G  G G C C A G G C G T  C G C A C G A G T G  C A C G G A G G C C  C T G C G G C C C C
      G C C C G T C G C C  G T C G C G A G C C  A C G C G A C G T G  G T C G G T G T G C  C C G G T C C G C A  G C G T G C T C A C  G T G C C T C C G G  G A C G C C G G C C

+1  P T T T  Q Q C  E A K C  D S P  T P G  D G P E  E C K  D V N
      TSPl-like Motif
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3281  C G A C T A C C A C  G C A G C A G T G T  G A G G C C A A G T  G C G A C A G C C C  A A C C C C C G G G  G A C G G C C C T G  A A G A G T G C A A  G G A T G T G A A C
      G C T G A T G G T G  C G T C G T C A C A  C T C C G G T T C A  C G C G T G C G G G  T T G G G G G C C C  C T G C C G G G A C  T T C T C A C G T T  C C T A C G C T T G

+1  K V A Y  C P L  V L K  F Q F C  S R A  Y F R  Q M C C  F T C
3361  A A G G T C G C C T  A C T G C C C C C T  G G T G C T C A A A  T T T C A G T T C T  G C A G C C G A G C  C T A C T T C C G C  C A G A T G T G C T  G C A A A A C C C T G
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3441  C C A G G G C C A C  T A G G G G G C G C  G C G G C A C C C G  G A G C C A C A G C  T G G C G G G G T C  T C C G C C G C C A  G C C C T G C A G C  G G G C C G G C C A
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3521  G A G G G G G C C C  C G G G G G G G G C  G G G A A C T G G G  A G G G A A G G G T  G A G A C G G A G C  C G G A A G T T A T  T T A T T G G G A A  C C C C T G C A G G
      C T C C C C C G G G  G C C C C C C C C G  C C C T T G A C C C  T C C C T T C C C A  C T C T G C C T C G  G C C T T C A A T A  A A T A A C C C T T  G G G G A C G T C C

3601  G C C C T G G C T G  G G A G G A T C C A  C C C C A A C C T C  T G C C C T G C C C  G C C C C A G G G G  C A C C C C G A C A  T C C A G G C C A C  C C C C T C A T G G
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3681  T G C T A C A G A C  C C T G C C C T G G  G G C C C A C A C A  C T C C T G C C A G  G A A G C C C T A C  A T C A A T A A A G  T T C T G T C T T G  T G T A G A T T T C
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3761  T A A A A A A A A A  A A A A A A
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Percent Homology

| Sim | Ident | 181 |
|-----|-------|----------------|
| 47 | 31 | |
| 45 | 31 | |
| 51 | 33 | |
| 73 | 59 | |
| 48 | 30 | |
| 49 | 33 | |
| 63 | 48 | (TS-4 v. TS-5) |

| Sim | Ident | 181 |
|-----|-------|----------------|
| 47 | 31 | |
| 45 | 31 | |
| 51 | 33 | |
| 73 | 59 | |
| 48 | 30 | |
| 49 | 33 | |
| 63 | 48 | (TS-4 v. TS-5) |

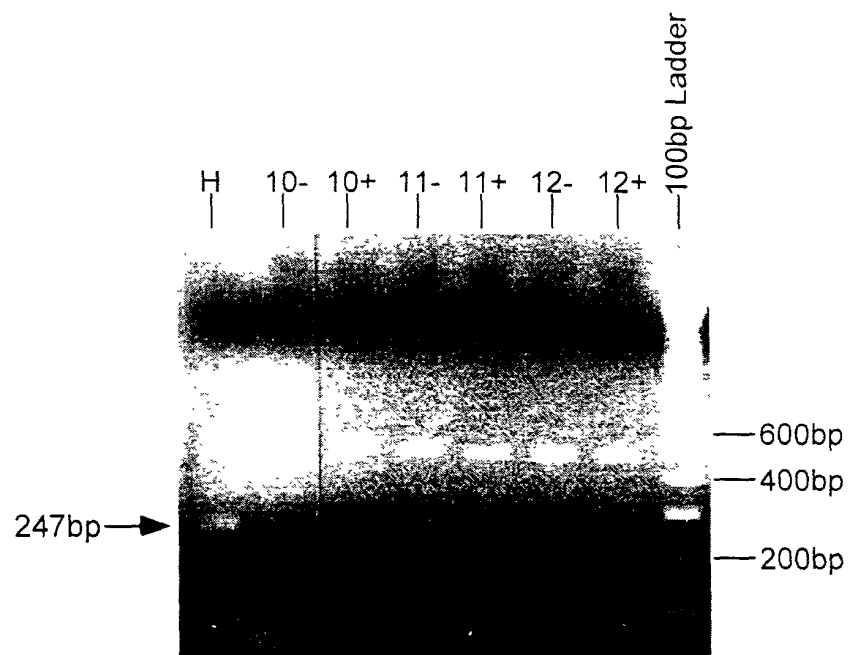


Figure 5. Expression of ADAMTS-E in cDNA from osteoarthritic cartilage.

Figure 6. Amino acid alignment of human ADAMTS-E with a GenScan prediction of ADAMTS-E from mouse genomic sequence.

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|-----------|-------|--|--|------|
| | | 1 | | 80 |
| hADAMTS-E | (1) | -----HASDGAEAPGAAQEPG--DAKAVNRGGGTGGAAGSRGWGETCGHVASMAPACQILRWALALG | | |
| mADAMTS-E | (1) | KMCDHSSYSPPFVPLLRLRVGNQCPLPKVDVKGTSDAAQTVNRGGSTVGAAASSRGWGETCGHVAPMASACQILRWALALG | | |
| Consensus | (1) | G P G DAA VNRGG TVGAA SRGWGETCGHVA MA ACQILRWALALG | | |
| | | 81 | | 160 |
| hADAMTS-E | (62) | LGLMFEVTHAFRSQDEFLSSLESYEIAFPTRVDHNGALLAFSPPPRRQRRTGATAESRLFYKVASPTSTHFLNLTPSS | | |
| mADAMTS-E | (81) | LGLTFKVTHAFRSQDELLSSLESYEIAFPTRVDHNGAMLAFFPPAFRRQRAGATTESRLFYKVAAPSTHFLNLTRSP | | |
| Consensus | (81) | LGL F VTHAFRSQDE LSSLESYEIAFPTRVDHNGA LAFSP RRQRAG GAT ESRLFYKVA PSTHFLNLTPS | | |
| | | 161 | | 240 |
| hADAMTS-E | (142) | RLLAGHVSVEYWTREGLAWQRAARPHCLYAGHLQQAQASTSHVAISTCGGLHGLIVADEEYLYIEPLHGGPKGSRSPSEESG | | |
| mADAMTS-E | (161) | RLLAGHVSVEYWTREGLAWQRAARAHCLYAGHLQQAQAGSSHAVSTCGGLHGLIVADDEEYLYIEPLQGGPKGHRGPEESG | | |
| Consensus | (161) | RLLAGHVSVEYWTREGLAWQRAAR HCLYAGHLQQA SHVA STCGGLHGLIVAD EYLYIEPL GGPGR R PEESG | | |
| | | 241 | | 320 |
| hADAMTS-E | (222) | PHVVYKRSSLRHPHLDTACGVDEKPKWGRPWRLTLKPPPARPLGNETERGQPGLKRSVSRERYVETLVVADKMMVAYH | | |
| mADAMTS-E | (241) | PHVVYKRSSLRHPHLDTACGVDEKPKWGRPWRLTLKPPPARPLGNESEERGQLKRSVSRERYVETLVVADKMMVAYH | | |
| Consensus | (241) | PHVVYKRSSLRHPHLDTACGVDEKPKWGRPWRLTLKPPPARPLGNE ERGQ GLKRSVSRERYVETLVVADKMMVAYH | | |
| | | 321 | | 400 |
| hADAMTS-E | (302) | GRRDVEQYVLAIMNIV-----AKLFQDSSLGSTVNILVTRLLILLTEDQPTLEITHHAGKSLDSFCKWQKSIVNHS | | |
| mADAMTS-E | (321) | GRRDVEQYVLAIMNITRSLFLGGQVAKLFQDSSLGNIVNILVTRLLILLTEDQPTLEITHHAGKSLDSFCKWQKSIVSHS | | |
| Consensus | (321) | GRRDVEQYVLAIMNI AKLFQDSSLG VNILVTRLLILLTEDQPTLEITHHAGKSLDSFCKWQKSIV HS | | |
| | | 401 | | 480 |
| hADAMTS-E | (372) | GHGNAIPENGVANHDTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCSVNEDIGLATAFTIAHEIGHTFTGMNHDGV | | |
| mADAMTS-E | (401) | GHGNAIPENGVANHDTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCSINEDIGLATAFTIAHEIGHTFTGMNHDGV | | |
| Consensus | (401) | GHGNAIPENGVANHDTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCS NEDIGLATAFTIAHEIGHTFTGMNHDGV | | |
| | | 481 | | 560 |
| hADAMTS-E | (452) | GNSCGARGQDPAKLMAAHITMKTNPFWSSCSRDIYITSLDSSLGLCLNNRPPRQDFVYPTVAPGQAYDADEQCRCFQHG | | |
| mADAMTS-E | (481) | GNGCGARGQDPAKLMAAHITMKTNPFWSSCSRDIYITSLDSSLGLCLNNRPPRQDFVYPTVAPGQAYDADEQCRCFQHG | | |
| Consensus | (481) | GN CGARGQDPAKLMAAHITMKTNPFWSSCSRDIYITSLDSSLGLCLNNRPPRQDFVYPTVAPGQAYDADEQCRCFQHG | | |
| | | 561 | | 640 |
| hADAMTS-E | (532) | KSRQCKYGEVCSSELWCLSKSNRCITNSIPAAEGTLCQTHIDKGWCYKRVCPVFGSRPEGVDGAWGPWPWGDCSRCTCGG | | |
| mADAMTS-E | (561) | KSRQCKYGEVCSSELWCLSKSNRCITNSIPAAEGTLCQTHIDKGWCYKRVCPVFGSRPEGVDGAWGPWPWGDCSRSCGG | | |
| Consensus | (561) | KSRQCKYGEVCSSELWCLSKSNRCITNSIPAAEGTLCQTHIDKGWCYKRVCPVFGSRPEGVDGAWGPWPWGDCSR CGG | | |
| | | 641 | | 720 |
| hADAMTS-E | (612) | GVSSSSRHCDSPRPTIGGKYCLGERRRHRSNTDDCPPGSQDFREVQCSEFDSIPFRGKFYKWKTYRGGGVKACSLTCLA | | |
| mADAMTS-E | (641) | GVSSSSRHCDSPRPTIGGKYCLGERRRHRSNTDDCPPGSQDFREMOCSEFDSVPFRGKFYKWKTYRGGGVKACSLTCLA | | |
| Consensus | (641) | GVSSSSRHCDSPRPTIGGKYCLGERRRHRSNT DCPGSGQDFRE QCSEFDS PFRGKFY WKTYRGGGVKACSLTCLA | | |
| | | 721 | | 800 |
| hADAMTS-E | (692) | EGNFYTERAAAVVDGTPCRPDTVDICVSGECKHVGCNDRVLGSDLRDCKRVCVGGDGSACETIEGVFSPASPGAGYEDVV | | |
| mADAMTS-E | (721) | EGNFYTERAAAVVDGTPCRPDTVDICVSGECKHVGCNDRVLGSDLRDCKRVCVGGDGSACETIEGVFSPALPGTG YEDVV | | |
| Consensus | (721) | EGNFYTERAAAVVDGTPCRPDTVDICVSGECKHVGCNDRVLGSDLRDCKRVCVGGDGSACETIEGVFSPA PG GYEDVV | | |
| | | 801 | | 880 |
| hADAMTS-E | (772) | WIPKGSVHIFIQDLNLSLSHLALKGDQESLLEGLPGTPQPHRLPLAGTTFQLRQGPDPQVQSLEALGPINASLIIMVLAR | | |
| mADAMTS-E | (801) | WIPKGSVHIFIQDLNLSLSHLALKGDQESLLEGLPGTPQPHRLPLAGTTFHLRQGPDPQVQSLEALGPINASLIIMVLAQ | | |
| Consensus | (801) | WIPKGSVHIFIQDLNLSLSHLALKGDQESLLEGLPGTPQPHRLPLAGTTF L RQGPDPQ QSLEALGPINASLI MVLAR | | |
| | | 881 | | 960 |
| hADAMTS-E | (852) | TELPALRYRFNAPIARDLPPYSWHYAPWTKSAQCAGGSQVQAVECRNQLDSSAVAPHYCSAHSKLPKRQRACNTEPCP | | |
| mADAMTS-E | (881) | AELPALHYRFNAPIARDLPPYSWHYAPWTKSAQCAGGSQVQVECRNQLDSSAVAPHYCSGHSKLPKRQRACNTEPCP | | |
| Consensus | (881) | ELPAL YRFNAPIARD LPPYSWHYAPWTKSAQCAGGSQVQ VECRNQLDSSAVAPHYCS HSKLPKRQRACNTEPCP | | |
| | | 961 | | 1040 |
| hADAMTS-E | (932) | PDWVVGNSLCSRSCDAGVRSRVSVCQRRVSAAEKALDDSDACQPRPPVLEACHGPTCPPEWAALDWSECTPSCGPGLR | | |
| mADAMTS-E | (961) | PDWVVGNSRCSRSCDAGVRSRVSVCQRRVSAAEKALDDSDACQPRPPVLEACQGPMPPEWATLDWSECTPSCGPGLR | | |
| Consensus | (961) | PDWVVGNS CSRSCDAGVRSRVSVCQRRVSAAEKALDDSDACQPRPPVLEAC GP CPPEWA LDWSECTPSCGPGLR | | |
| | | 1041 | | 1120 |

